REMARKS/ARGUMENTS

The Office required restriction of Claims 18-29, 31, 36 and 37 to one of the following exemplary groups, or to a group outside of these groups in accordance with the Examiner's comments on pages 10 and 11 of the present Office Action.

Group I: Claims 18-27, drawn to products of the formula (I), wherein
R1 is aryl, optionally substituted by (A1)-(A32), as defined in claim 21
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group II: Claims 18-27, drawn to products of the formula (I), wherein
R1 is aryl, optionally substituted by (A1)-(A32), as defined in claim 21
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group III: Claims 18-27, drawn to products of the formula (I), wherein
R1 is lower alkyl or halogen
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group IV: Claims 18-27, drawn to products of the formula (I), wherein
R1 is lower alkyl or halogen
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene

m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group V: Claims 18-27, drawn to products of the formula (I) wherein
R1 is furyl, optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group VI: Claims 18-27, drawn to products of the formula (I), wherein
R1 is thienyl, optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group VII: Claims 18-27, drawn to products of the formula (I), wherein
R1 is morpholinyl, optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group VIII: Claims 18-27, drawn to products of the formula (I), wherein
R1 is furyl, optionally substituted by a group selected form the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene

m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group IX: Claims 18-27, drawn to products of the formula (I), wherein
R1 is thienyl, optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group X: Claims 18-27, drawn to products of the formula (I), wherein
R1 is morpholinyl, optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XI: Claims 28 and 31, drawn to processes for the preparation of products of the formula (I), wherein
R1 is aryl, optionally substituted by (A1)-(A32), as defined in claim 21
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XII: Claims 28 and 31, drawn to processes for the preparation of products of the formula (I), wherein
R1 is lower alkyl or halogen
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene

m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XIII: Claim 36, drawn to processes for the preparation of products of the formula (I), wherein
R1 is aryl, optionally substituted by (A1)-(A32), as defined in claim 21
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XIV: Claim 36, drawn to processes for the preparation of products of the formula (I), wherein
R1 is lower alkyl or halogen
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XV: Claims 29 and 37, drawn to methods of treating arthritis with the products of the formula (I), wherein
R1 is aryl optionally substituted by (A1)-(A32) as defined in claim 21
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XVI: Claims 29 and 37, drawn to methods of treating HIV-infection with the products of the formula (I), wherein
R1 is lower alkyl or halogen
R2 is carboxy
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene

m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

Group XVII: Claims 29 and 37, drawn to methods of treating sepsis with the products of the formula (I), wherein
R1 is furyl optionally substituted by a group selected from the group consisting of (B1) to (B8), as defined in claim 20
R2 is carboxy
Ar is thienyl
A is ethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

On pages 10-11 of the present Office Action, the Examiner provided that an election (a product, a process or a method of use) outside of listed exemplary Groups I-XVII is allowed, by identification of another specific embodiment, not listed in Groups I-XVII, or by choosing a single invention (a product, a process, or a method of use), along with a single disclosed species. Applicants now provide an election outside of the exemplary Groups I-XVII.

Applicants elect, with traverse, the following product for continued prosecution:

Claims 18-27, drawn to products of the formula (I), wherein
R^1 (or R1) is phenyl, optionally substituted by (C1)-(C31), as defined in claim 23
R^2 (or R2) is carboxy or hydroxyaminocarbonyl
Ar is thienyl
A is trimethylene
X is a single bond
Y is thia, sulfinyl or sulfonyl
Z is methylene
m and n are each an integer of 0 to 6, and 1 is less than or equal to (m+n) which is less than or equal to 6, and salts thereof.

The Examiner has asserted, on page 11 of the present Office Action, that the claims herein lack unity of invention under PCT Rule 13.1 and PCT Rule 13.2, since under 37 CFR 1.475(a), the compounds defined in the claims, lack a significant structural element,

qualifying as the special technical feature that defines a contribution over the prior art. The Examiner also asserted that the vastness of the claimed subject matter, and the complications in understanding the claimed subject matter, impose a serious burden on any examination of the claimed subject matter. The Examiner further asserted that unity of invention is lacking, based on 37 CFR 1.475(a)-(c) and (e), as noted on pages 11 and 12 of the present Office Action. Thus, the Examiner required restriction among the above groups. Applicants respectfully traverse based on the following reasons.

The MPEP provides guidelines for the determination of a "lack of unity of invention" between restricted Groups. MPEP §1893.03(d) states:

> When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature in each group.

The Examiner has provided a general conclusion, as provided on page 11 of the present Office Action, that the claims lack a significant structural element, qualifying as the special technical feature, and that the technical feature of the instant claims is a CH_2 group, which does not define a contribution over the art, as can be seen by the references on the submitted 1449 form, and that the variables on the CH_2 group vary extensively, and result in vastly different compounds. However, the Examiner has not provided a proper determination as to why the claims lack unity with each other, in terms of a specific description of the unique technical feature in each exemplary group. Moreover, Claims 1-36 share a common structural feature of the compound represented by formula (I) (Applicants note the error in Claim 37, and will amend this claim upon further prosecution of the present application).

In addition, the PCT administrative instructions in the MPEP, Annex B, Part 1(f) define Markush practice, and provides that the alternatives defined in a single claim shall meet the technical relationship requirements of PCT Rule 13.2, if they are of a similar nature.

These alternatives shall be regarded as being of a similar nature, when the following criteria are fulfilled:

(A) all the alternatives have a common property or activity, and

(B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

Applicants submit that each of the alternatives share a common activity: metalloproteinase inhibition. In addition, each alternative has a common structure: formula (I). Accordingly, criteria (A) and (B)(1) are met, and the alternatives are of a similar nature as that term is defined in Annex B above.

Applicants traverse that Restriction Requirement on the additional grounds that the Office has not applied the same standard of unity of invention as the International Authority. The Authority did not take the position that unity of invention was lacking in the International Preliminary Examination Report (IPER), with respect to original Claims 1-17, which are similar in scope to the now pending claims, and examined all claims together. Applicants note that PCT Article 27(1) states:

> No national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations.

Moreover, Applicants respectfully traverse on the grounds that the Office has not shown that a burden exists in searching the entire application. Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office. In fact, the International Authority has searched all of the claims together, and did not find unity of invention lacking (see IPER and International Search Report).

The Examiner has also asserted on pages 11 and 12 of the present Office Action, that even if unity of invention under 37 CFR 1.475(a) is not lacking, under 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product; or
(2) A product and a process of use of said product; or
(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
(4) A process and an apparatus or means specifically designed for carrying out the said process; or
(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

The Examiner further asserted that according to 37 CFR 1.475(c), "if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present." The Examiner concluded that since the claims are drawn to more than a product, a process and more than a method of use, and that since, according to 37 CFR 1.475(e), "the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim," the present claims lack unity of invention, and should be limited to only a product or a process or a use of the said product.

The Examiner provided only a general statement that the claims of the present application are drawn to more than a product, a process and more than a method of use, without providing any reasons to support this statement. In the absence of such support, and in light of the finding of the International Authority, the Examiner has not shown a lack of unity of invention.

Thus, the Examiner has not supported the restriction of the claims, and has not shown that it would be a serious burden to search and examine all the claims together. Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office.

Applicants also respectfully submit that if the elected product claims are found allowable, withdrawn method claims should be rejoined under MPEP § 821.04, if the method claims depend on, or include all the limitations of, the respective allowed product claim.

Finally, Applicants respectfully submit that it appears the above restriction represents an election of species, and therefore, should the elected species (product) be found allowable, the Office should expand its search to the non-elected species within the broader representation of the elected product.

Accordingly, for at least the above reasons, Applicants submit that the Office has not met the requirements to sustain a restriction in the present application. Applicants respectfully request the withdrawal of the Restriction Requirement.

Respectfully submitted,

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